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SLIDE FORUM—CVS/ECMO 3: CONTINUOUS FLOW PUMPS FOR CIRCULATORY SUPPORT

The Sternotomy Hemopump

A Second Generation Intraarterial Ventricular Assist Device

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The first generation Hemopump is a VAD based on a catheter mounted intraarterial axial flow blood pump that is placed through the femoral artery. Blood is withdrawn from the left ventricle through a transvalvular inflow cannula and pumped into the aorta. Clinical trials have demonstrated hemodynamic efficacy, improved survival, and low hemolysis in cardiogenic shock. The incidence of non-insertion of the device and fracture of the flexible drive cable limited its utility, however. In addition, some processes used in pilot production could not be adapted to volume manufacturing. A second generation device, the Sternotomy Hemopump, has been developed for insertion through the ascending aorta. Design changes include a shortened inflow cannula, higher flow hydraulics, and a more durable flexible drive cable. In addition, more efficient manufacturing processes were implemented. In a pulsatile mock loop the flow was 5.7 L/min at 100 mmHg. *In vivo* experiments of up to 2 weeks demonstrated a mean plasma free hemoglobin of 8.7 mg/dl, minimal valve injury, and an acceptable incidence of renal infarction. *In vitro* endurance demonstrated a 7 day reliability of 99.9% with a 95% confidence. A new clinical trial will evaluate the use of the Sternotomy Hemopump for nonoxygenator support during aorto-coronary artery bypass surgery. *ASAIO Journal* 1993; 39: M218–M223.

The first generation Hemopump device (HP100) is a catheter mounted intra-arterial ventricular assist device (VAD) based on a miniaturized axial flow blood pump, and intended for surgical placement through the femoral or iliac artery. This device, which was described to the society in 1988,[1] was first used clinically for the treatment of cardiogenic shock by O. H. Frazier *et al.* in 1988. The results of a U.S. clinical trial, which evaluated the utility of the HP100 Hemopump system in the treatment of cardiogenic shock,[2] demonstrated a significant hemodynamic response and, in selected patients, left ventricular recovery and improved survival. A number of device failures that were observed during the clinical trial, however, limited the effectiveness of this device and required corrective action. The sum of these changes have culminated in a second generation device, the Sternotomy Hemopump (HP31).

The HP31 device, shown in **Figure 1,** is a disposable pump assembly designed for placement through the ascending or transverse aorta through a sternotomy incision. This device is 9.5 cm in length and 8 mm (24 Fr.) in diameter. At a shaft speed of 26,000 RPM and a pulsatile delta pressure across the pump of 100 mmHg, it can deliver 5.7 L/min of flow. During use it is positioned such that the inflow cannula traverses the aortic valve to provide direct removal of blood from the left ventricle. The pumping mechanism resides in the ascending aortic arch and expels blood into the systemic circulation. Rotary motion is supplied to the pump through a motor driven flexible drive cable. Electric power is supplied to the external motor by an electronic controller, which also assesses system performance.

Following is a description of the evolutionary process and methods used to develop and validate the design changes that have been incorporated into the Hemopump system to improve its performance and reliability.

Method

Between April 1988 and November 1991, a clinical trial was conducted in the United States to evaluate the safety and efficacy of the Hemopump system in the treatment of cardiogenic shock. Selected information from this trial was used to identify device problems that occurred during clinical testing. The safety and reliability of the device was determined by evaluating patient complications, device related adverse events, and equipment failures reported during the U.S. clinical trial. In addition, all devices were returned for engineering evaluation to determine the cause of any failures. The engineering inspection included gross visual and photographic evaluation, and disassembly of the pumps to examine each component for wear, damage, and presence of debris or blood. Detailed audits were also conducted to determine if failed devices were clustered in certain production lots and to verify that adequate control of processes and material had been maintained during production.

If a particular equipment failure was observed to be a recurring problem, then this failure was simulated *in vitro* in

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Figure 1. Sternotomy Hemopump System (Courtesy of JJIS, Rancho Cordova, CA).

mock circulatory loops or in component tests, whenever possible. In this way, the precise mode of failure could be determined.

If an improvement in the design was needed, the development group identified and executed testing of various concepts. These concepts then were evaluated with the aid of mechanical testing using the *in vitro* models. Promising design changes were evaluated *in vivo* during chronic implantation in animals. Design changes that were subsequently implemented were subjected to a rigorous preclinical qualification program to evaluate performance, durability, and safety to justify use of the new device in humans. This preclinical qualification consisted of three tests: 1) *in vitro* performance testing, 2) *in vitro* endurance testing, and 3) chronic *in vivo* experiments.

In Vitro *Performance Testing*

The purpose of this test was threefold: 1) to determine Sternotomy Hemopump system operating characteristics over the range of heart rates and aortic pressures anticipated in the clinical trial, 2) to validate that the Sternotomy Hemopump system provides physiologically significant flow over a wide range of hemodynamic conditions, and 3) to identify operating parameters (delta pressure, heart rate, and pump rate) that will result in cyclic stress equivalent to or greater than those anticipated in patients. These findings were used to identify operating conditions for *in vitro* endurance testing.

This test was conducted by running four HP31 Sternotomy Hemopump systems in a pulsatile mock circulatory loop. System response was observed and recorded, including heart rate, pump rate, aortic pressure, delta pressure across the pump, loop flow, mean motor current, motor current pulse amplitude, motor voltage, and purge pressure.

In Vitro *Endurance Testing*

The *in vitro* endurance test was designed to demonstrate the reliability of the HP31 Sternotomy Hemopump assembly, when subjected to operating conditions equal to or more stressful than those expected during clinical use. Eight HP31 pumps were tested in a mock circulatory loop. In addition, four Phase I HP100S (dual layer drive cable, O-ring seal loading, and cast hydraulics) Hemopump assemblies, were tested under the same conditions to serve as controls and to validate the severity of the endurance test conditions. The testing environment was designed to mimic the conditions of an implantation of the device through a 2" graft anastomosed, at a 45° angle, to the ascending aorta. The cannula then was placed retrograde across a prosthetic valve into a mock ventricle. The hemodynamic conditions of the mock circulatory loop, listed below, were based on the results of the performance testing and Phase I clinical trials. The operating conditions of the endurance loop were: 1) cyclic change in delta pressure across the pump of 90–100 mmHg, 2) heart rate of 100–110 BPM, 3) aortic pressure of 150/100, and 4) pump rate 7.

In Vivo *Testing*

The purpose of the *in vivo* qualification testing was to validate the safety and durability of the HP31 Sternotomy Hemopump assembly, when implanted in the biologic environment. Eight chronic (14 day) experiments in the ovine model were attempted. The pump assembly was surgically placed by thoracotomy in six and the carotid artery in two. Complete blood counts, platelets, and blood chemistries were evaluated before implantation and throughout the period of assistance until termination of the experiment. Pump performance, including purge pressure, seal flow, and motor current, was recorded. Alarm conditions were recorded and corrected when possible. All animals underwent a complete post mortem evaluation and samples of organs were submitted for histopathologic examination. All explanted pumps were examined for signs of thrombodeposition, evidence of wear, and signs of failure.

Results

One hundred fourteen patients were accepted for treatment with the Hemopump during the clinical trial in the United States. Three device related adverse events or device

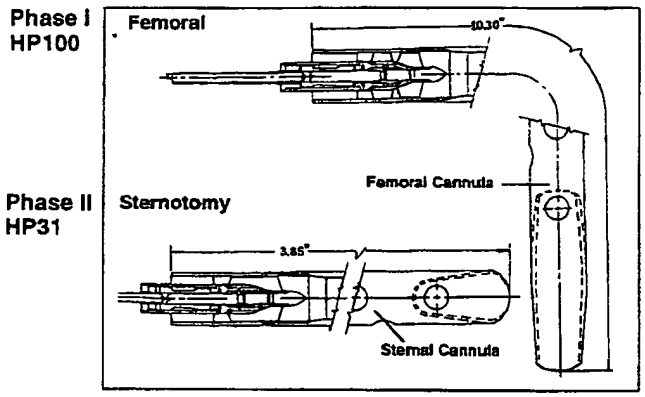

Figure 2. Hemopump cannulas: femoral and sternotomy (Courtesy of JJIS, Rancho Cordova, CA).

failures were identified for potential design changes that included: 1) failure to insert the Hemopump device in 24% of patients, 2) fracture of the flexible drive cable in 9.4%, and 3) a faulty rotating seal (1.7%) requiring replacement of the Hemopump. In addition, the process used to fabricate the hydraulic elements of the axial flow pump proved impractical for high volume production. The history of the device problem, the rationale of the design change, and the results of qualification are summarized below.

Non-Insertion

The Femoral Hemopump (HP100) could not be inserted in 24% of the patients accepted into the Phase I trial. Non-insertion of the Hemopump was, primarily, caused by small caliber and atherosclerosis of the illeofemoral system. To minimize non-insertion in surgical patients, a change in strategy was implemented: a Hemopump intended for placement in the ascending or transverse aorta through a median sternotomy was created. This approach obviated problems related to the size of the illeofemoral vessels. A device configured for sternotomy placement required a shortened inflow cannula (3.85 inches) compared with the Femoral Hemopump (10.3 inches). The cannulas for the sternotomy pump and the femoral pump are shown in **Figure 2.**

Drive Cable Fracture

The incidence of drive cable fracture in the femoral pump assembly was 9.4%. These fractures were associated with a bend radius of less than 2 inches. In an early version of the Sternotomy Hemopump (HP100S), the fracture rate was 60%. Initial efforts to simulate drive cable fractures in a non-pulsatile mock circulatory loop were unsuccessful in spite of the presence of bend radii less than 2 inches. It was only when pulsatile pressure was added to the test conditions that the drive cable fractures could be replicated *in vitro*. Engineering evaluation of the mode of the drive cable failure indicated that a more flexible cable was needed; one that could withstand the small bend radius and high cyclic stresses that occur during clinical use. Such a drive cable was developed based on a tri-layer design, and has been incorporated into the HP31 Sternotomy Hemopump assembly. It offers marked improvement in durability compared with the dual layer drive cable used in the HP100. **Figure 3** illustrates a comparison between the dual layer drive cable of the HP100 and the trilayer drive cable of the HP31.

Precision Metallic Spring

In order to maintain seal integrity, the rotating shaft seal is flushed with purge fluid (40% dextrose and water) to prevent entry of blood elements into the pump bearings. An adequate compressive force must be applied to the seal assembly and maintained if it is to function effectively during use. The seal load was originally applied by compressing an O-ring with an adjustment nut. The O-ring has been associated with variability and instability in the sealing characteristics of pump assemblies. Loss of seal function can result in a loss of purge pressure and subsequent entry of blood into the pump bearings. In addition, shelf life was limited because of decay in the performance of the O-ring. The ideal loading mechanism for the seal would be insensitive to aging, radiation, and moisture and would permit quantitative verification of the applied load during assembly.

A precision metallic spring is now used to apply the preload to the seal. The O-ring and threaded adjustment nut have been eliminated. One end of an integral spring is bonded to the pump shaft to maintain the seal load. A load cell fixture is used to compress the spring to a predetermined seal load before bonding the spring to the pump shaft **(Figure 4).**

Hydraulic Elements: Rotor and Stator

During the Phase I clinical trial, the blade geometry of the hydraulic elements (rotor and stator) of the pump assembly were fabricated by a lost wax casting process. Although lost wax casting did produce satisfactory parts, small inclusions formed during casting resulted in very poor yields and inconsistent parts. Because the lost wax casting process could not economically produce large volumes of parts, manufacturing engineers sought a new way to produce rotors and stators. The new process needed to be very reproducible,

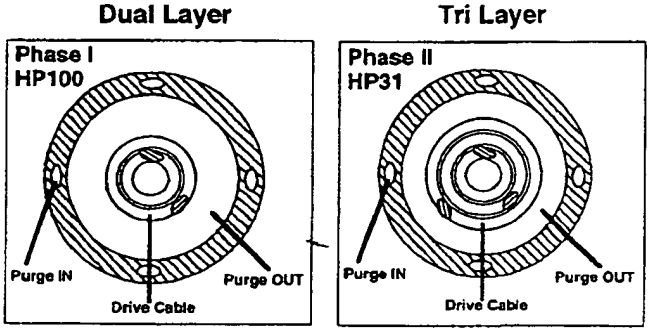

Figure 3. Comparison of the cable/sheath assembly (Courtesy of JJIS, Rancho Cordova, CA).

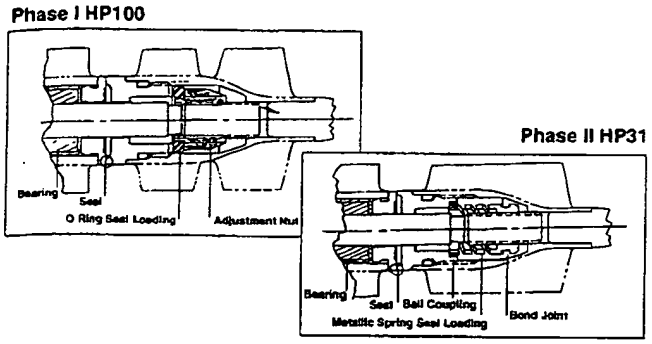

Figure 4. Comparison of seal loading mechanisms (Courtesy of JJIS, Rancho Cordova, CA).

adaptable to volume production, and offer equivalent or greater hemodynamic support compared to the cast parts. In addition, hemolysis and thromboresistance could not be compromised. A new design, based on a helicoidal blade design, has been developed. These hydraulic components are now fabricated on a computer numerically controlled (CNC) mill that has been modified to machine production quantities of rotors and stators for the Sternotomy Hemopump. Computer machining of the hydraulic elements has a number of advantages: 1) the tolerances achieved with the CNC mill result in much greater uniformity from part to part and batch to batch than with the lost wax casting process, 2) inclusions or voids are rarely found because parts are machined from worked stock rather than poured metal, and 3) less hand polishing is required because the machined parts have a smoother finish compared with the raw castings.

The resulting machinable design has demonstrated improved hydraulic performance compared with the cast hydraulic design and does not compromise hemolysis or thromboresistance. The two designs are compared in **Table 1.**

Qualification Testing of the Sternotomy Hemopump

In Vitro Performance Testing. A summary of hydraulic performance of the Sternotomy Hemopump is shown in **Table 2.** The pump produced flows from 1.23 to 7.06 L/min. These results include delta pressures across the pump of 150 mmHg, which is in excess of pressures anticipated in healthy patients or in candidates proposed for assistance in the Phase II trial. Based on a normal cardiac output of 6.0 L/min, the Sternotomy Hemopump demonstrated an ability to provide 100% of the cardiac output.

The cyclic stress on the system, as measured by the magnitude of the current pulse amplitude, was found to most directly relate to the cyclic pressure gradient (delta pressure) across the pump. These results are summarized in **Table 3.** They indicate that the current pulse amplitude increases significantly in a linear fashion with delta pressure. No correlation between heart rate and current pulse amplitude was observed.

For *in vitro* endurance testing, the recommended operating parameters that will result in cyclic stress equivalent to or greater than that anticipated in patients in a clinical setting are as follows:

Cyclic Delta Pressure across the pump	90–100 mm Hg
Aortic Pressure	150/100
Heart Rate	100–110 beats per minute
Pump Rate	7 (except for brief wean cycles)

In Vitro Endurance Testing. The HP31 tri-layer pumps failed between 26 and 58 days. Six pumps failed because of flexible drive cable fracture and two because of flex sheath deterioration. All four control pumps (HP100 with dual layer drive cables) failed in less than 35 hours due to drive cable fracture. Estimates of mean and median time to failure (MTTF) were calculated for both pump designs. These MTTF values establish an estimate of device reliability at the end of the intended period of use (7 days) of 99.9% for the HP31 pump and 0% for the HP100S **(Table 4).** All reliability estimates were evaluated at 95% confidence.

In Vivo Testing. Insertion of the HP31 Sternotomy Hemopump assembly into the left ventricle and recovery from anesthesia was uneventful in all experiments. Two of the eight experiments were terminated at 2 days secondary to non-

Table 1. Comparison of Hydraulic Elements

	Phase I, HP100	Phase II, HP31
Manufacturing process	Cast	Machined
Rotor blade configuration	2 rows in series	1 row
Stator blade configuration	1 row	1 row
Hydraulic performance (nonpulsatile)	3.1 L/min 26.0 Krpm & 70 mmHg	4.7 L/min 26.0 Krpm & 70 mmHg
Free hemoglobin (*in vivo*)	6.6 mg/dl	8.7 mg/dl

Table 2. Variance in Pump Flow (L/min) as Pump Rate and Delta Pressure Change

	Delta Pressure (mmHg)			
Pump Rate	50	75	100	150
1	3.5	2.9	2.2	1.2
3	4.7	4.1	3.5	2.4
5	5.9	5.3	4.6	3.6
7	7.1	6.5	5.8	4.8

Table 3. Variance in Current Pulse Amplitude as Pump Rate and Delta Pressure Changes

	Delta Pressure (mmHg)			
Pump Rate	50	75	100	150
1	0.037	0.053	0.071	0.102
3	0.030	0.046	0.066	0.094
5	0.023	0.039	0.058	0.087
7	0.016	0.032	0.052	0.080

Table 4. Comparison of Mean and Median Time to Failure

	Time to Failure (days)		Reliability R(7)
Model No.	Mean	Median	95% Confidence
HP31	38.1	38.3	99.9%
HP100S	0.61	<1	0%

pump related complications: massive lymph leak into the chest cavity from surgical injury to the thoracic duct, and portal vein thrombosis from gas forming organisms. Only one experiment was terminated early from a pump related problem; a torque coupling failed at 12 days because of a bond failure. No focal neurologic events suggestive of stroke or transient ischemic attack were observed. **Table 5** summarizes the mean values of the complete blood counts and blood chemistries before pump insertion and during pump operation.

Post mortem evaluation demonstrated no clinically significant pump related adverse effects. In one animal there was clinically insignificant endocardial abrasion, in two animals clinically significant renal infarcts were noted, one associated with probable sepsis, the other with insufficient anticoagulation. Two animals were killed or died because of surgically related complications. 1) fatal portal vein thrombosis, and 2) chylothorax from laceration of the thoracic duct. In all animals the aortic valves were unremarkable and no infarcts of the brain were noted. No deaths were thought to be caused by the Hemopump system.

Device Performance. Five experiments ran 14 days, one 12 days, and two 2 days. No drive cable failures were observed in the experiments. One device failed on the 12th day because of a bond failure that was traced to use of an improper adhesive in an early pilot production lot. Steps have been implemented to ensure that the proper adhesive is used. There were no other failures of pump assemblies. Expulsion of the cannula from the left ventricle did not occur. Tearing of the inflow cannula was not observed. Postexplant inspection of the pumps showed no evidence of thrombodeposition.

Summary of Qualification Testing

The Hemopump system provides physiologically significant flow over a wide range of hemodynamic conditions. Based on the results of the *in vitro* endurance study, it is expected that the durability of the HP31 pump assembly will be improved significantly compared with the HP100S. The results of the *in vivo* experiments suggest that acceptable levels of hemolysis, anatomic injury, and thromboembolic sequelae can be expected in the absence of sepsis and with the recommended level of anticoagulation. The Sternotomy Hemopump system should have an excellent rate of insertion, a low incidence of mechanical failure, and pose minimal risk during clinical use.

Discussion

Unfortunately, it is not possible to anticipate all potential device failures because of the inherent limitations of preclinical *in vitro* and *in vivo* evaluation; there are, after all, many differences between men and sheep. Consequently, the development of a medical device cannot be considered complete until the device failures and equipment problems that occur in clinical use are identified and resolved. This is a slow, painful process that cannot be avoided nor easily shortened. There are, however, several principles that must be fully embraced by the organization, otherwise all hope of success must surely be abandoned. First, a strict manufacturing discipline must take over once development's job is "complete." Tight, even tyrannical control of processes and materials must be maintained during qualification and clinical trials. I am not convinced that this can be overdone. It must be said that development engineers (yes, even I) are poorly suited to such discipline. If left unsupervised to play in the manufacturing area, development engineers will most certainly wreak havoc as they continue to perform undocumented "tweaks and adjustments" on hardware. There is nothing more frustrating than learning, after the fact, of some "insignificant" uncontrolled change that somehow crept into a frozen design, only later to be implicated in a device failure. Second, ongoing assessment of the performance and failures of the device in the field is critical to success. Engineers should visit the clinical sites on a continuing basis to talk with users and support personnel. Third, *in vitro* modeling of device failures is critical to successful resolution of design problems, particularly during qualification testing. Such models provide a meaningful way to compare designs in a carefully controlled, scientifically valid study.

In truth, though, the development process is never completely finished. There are always improvements to be

Table 5. *In Vivo* Blood Count Values and Blood Chemistries

	Preinsertion	24 hr	14 days
Free hemoglobin (mg/dl) (change from baseline)	—	12.45 ± 8.22	2.89 ± 5.48
Platelets (×1000)	452 ± 64	350 ± 33	560 ± 171
Creatinine (mg/dl)	1.21 ± 0.03	1.51 ± 0.09	1.24 ± 0.08
BUN (mg/dl)	25.13 ± 1.27	22.13 ± 2.03	21.60 ± 4.01
Total bilirubin (mg/dl)	0.06 ± 0.02	0.11 ± 0.01	0.12 ± 0.02
Alkaline phosphatase (IU/L)	88 ± 7	76 ± 6	56 ± 3
SGOT (IU/L)	86.75 ± 9.69	214.50 ± 29.99	102.40 ± 15.89

made, manufacturing processes to refine, and future devices to evolve. Even as the Sternotomy Hemopump approaches clinical trials, the 14 Fr. Percutaneous Hemopump is nearing pre-clinical qualification testing. Balancing the inventive fervor of the development group against the discipline and rigid structure of an effective manufacturing group is a challenge that can bring middle management to its knees and has hastened the death of many good devices.

One might reasonably inquire as to our plans for the future of the Sternotomy Hemopump. There is room to say only this. The Sternotomy Hemopump has been used successfully in pilot studies to evaluate its efficacy in providing non-oxygenator support during aortocoronary bypass. If successful it should be possible to avoid many of the complications of cardiopulmonary bypass and potentially lower the cost of ACB surgery. At this writing, clinical trials have begun in Europe and are pending in the United States. Preliminary results will be forthcoming.

Conclusion

Four very successful design changes have been incorporated into the Hemopump to result in the Sternotomy Hemopump system. This second generation device has much better hydraulic performance, is more reliable, has fewer adverse effects in animals, and has the potential to be less costly to produce. It now remains to demonstrate the clinical utility of the Hemopump so that it may find its proper place in the treatment of heart disease.

References

1. Wampler RK, Moise JC, Frazier OH, Olsen DB: *In vivo* evaluation of a peripheral vascular access axial flow blood pump. *Trans Am Soc Artif Intern Organs* 34: 450–454, 1988.
2. Wampler RK, Frazier OH, Lansing AM, et al: Treatment of cardiogenic shock with the left ventricular assist device. *Ann Thorac Surg* 52: 506–513, 1991.